Targeted bisulfite sequencing reveals changes in DNA methylation associated with nuclear reprogramming.

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Public Summary:

Scientific Abstract:
Current DNA methylation assays are limited in the flexibility and efficiency of characterizing a large number of genomic targets. We report a method to specifically capture an arbitrary subset of genomic targets for single-molecule bisulfite sequencing for digital quantification of DNA methylation at single-nucleotide resolution. A set of ~30,000 padlock probes was designed to assess methylation of ~66,000 CpG sites within 2,020 CpG islands on human chromosome 12, chromosome 20, and 34 selected regions. To investigate epigenetic differences associated with dedifferentiation, we compared methylation in three human fibroblast lines and eight human pluripotent stem cell lines. Chromosome-wide methylation patterns were similar among all lines studied, but cytosine methylation was slightly more prevalent in the pluripotent cells than in the fibroblasts. Induced pluripotent stem (iPS) cells appeared to display more methylation than embryonic stem cells. We found 288 regions methylated differently in fibroblasts and pluripotent cells. This targeted approach should be particularly useful for analyzing DNA methylation in large genomes.